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Dear Doctor Heidelberger:

Mulling over the sort of thing that we talked of the other day, I have come on a question which I realize has been in the back of my mind for some time but which I wasn't bright enough to get into the conversation with you.

Isn't it true that information as to the presence of antibodies in the living host and deductions as to their significance are based wholly upon circulating, free antibodies? And if so, how does one know that the deductions are not distorted by uncertainty as to the physiological significance of circulating, free antibody? What is the relation of circulating, free antibody to the antibody which conceivably has already done its work? Is it just a safety factor, a physiological overflow, or what? Would this account for the late rise of antibody titer in recovery from acute infection, and should one postulate a period before antibody becomes demonstrable when it may nevertheless be effectively reacting with antigen in the blood stream or conceivably within cells? When one measures potential resistance in terms of antibody titer, is one really measuring the physiological vagaries of one organism as compared with another in its capacity to produce an excess of a needed substance? Are there any instances in which one can recover and demonstrate not free antibody but the product of an antigen-antibody reaction - I mean, of course, in vivo?

Probably I'm greatly exaggerating a difficulty which doesn't exist, but if so I'm sure you can set me straight very quickly. With many thanks, as always, I am

Dr. Michael Heidelberger
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and Surgeons
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Yours sincerely,

Leeds Mich

GS EW

It was kind of you to give me so much time.